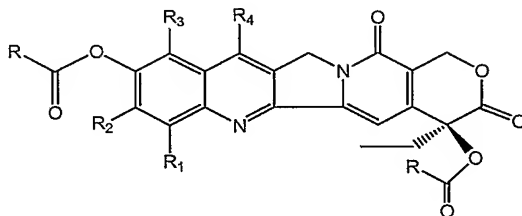


## WHAT IS CLAIMED IS:

1. A di-ester derivative of camptothecin having the following general structure:



wherein

$R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$ , which can be the same or different, are hydrogen, halogen,  $C_1$ - $C_{20}$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_4$ - $C_{20}$  aryl, and  $C_1$ - $C_{20}$  silyl,

each  $R$  can be the same or different and is  $C_1$ - $C_{30}$  alkyl,  $C_2$ - $C_{22}$  alkenyl,  $C_4$ - $C_{30}$  aryl,  $(CH_2)_nOR_5$ ,  $(CH_2)_nSR_5$ ,  $(CH_2)_nNR_5R_6$ ,  $(CH_2)_nCOR_7$ ,

wherein,

$R_5$  and  $R_6$ , which can be the same or different, are  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_6$  alkenyl, and  $C_4$ - $C_{10}$  aryl,

$R_7$  is hydroxy,  $C_1$ - $C_{20}$  alkyl,  $C_1$ - $C_6$  alkenyl,  $C_1$ - $C_6$  alkoxy,  $C_4$ - $C_{20}$  aryl, or  $NR_8R_9$ ,

wherein,

$R_8$  and  $R_9$ , which can be the same or different are  $C_1$ - $C_6$  alkyl,

and  $n$  is an integer of 1 to 8,

and pharmaceutically acceptable salts hereof.

2. A compound of claim 1 wherein each  $R$  can be the same or different and is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_6$  alkenyl, or  $C_4$ - $C_{20}$  aryl.

3. A pharmaceutical composition, comprising an effective amount of the camptothecin di-ester derivatives of claim 1 and a pharmaceutically acceptable carrier or diluent.

4. A pharmaceutical composition, comprising an effective amount of the camptothecin di-ester derivatives of claim 2 and a pharmaceutically acceptable carrier or diluent.

5. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is H, and R is  $C_3$ - $C_{30}$  alkyl.
6. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is H, and R is  $C_1$ - $C_{20}$  alkyl.
7. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is H, and R is  $C_2$ - $C_{22}$  alkenyl.
8. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  is H, and R is  $C_2$ - $C_6$  alkenyl.
9. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(CH_2)_nOR_5$ ,  
wherein,  
 $R_5$  is  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl, or  $C_4$ - $C_{10}$  aryl, and  
 $n$  is an integer of 1 to 2.
10. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(CH_2)_nSR_5$ ,  
wherein,  
 $R_5$  is  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl, or  $C_4$ - $C_{10}$  aryl, and  
 $n$  is an integer of 1 to 2.
11. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(CH_2)_nNR_5R_6$ ,  
wherein,  
 $R_5$  and  $R_6$  are independently hydrogen,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl, or  $C_4$ - $C_{10}$  aryl,  
and  
 $n$  is an integer of 1 to 2.
12. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(CH_2)_nCOR_7$ ,  
wherein,  
 $R_7$  is hydroxy,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl, or  $C_4$ - $C_{10}$  aryl, and

n is an integer of 2 to 4.

13. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $\text{C}_1\text{--C}_{30}$  alkyl.

14. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $\text{C}_1\text{--C}_{20}$  alkyl.

15. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $\text{C}_2\text{--C}_{22}$  alkenyl.

16. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $\text{C}_2\text{--C}_6$  alkenyl.

17. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $\text{C}_4\text{--C}_{30}$  aryl.

18. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $\text{C}_4\text{--C}_{20}$  aryl.

19. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $(\text{CH}_2)_n\text{OR}_5$ ,

wherein,

$R_5$  is  $\text{C}_1\text{--C}_6$  alkyl,  $\text{C}_2\text{--C}_6$  alkenyl, or  $\text{C}_4\text{--C}_{10}$  aryl, and

n is an integer of 1 to 2.

20. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $(\text{CH}_2)_n\text{SR}_5$ ,

wherein,

$R_5$  is  $\text{C}_1\text{--C}_6$  alkyl,  $\text{C}_2\text{--C}_6$  alkenyl, or  $\text{C}_4\text{--C}_{10}$  aryl, and

n is an integer of 1 to 2.

21. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $\text{CH}_2\text{CH}_3$ , and R is  $(\text{CH}_2)_n\text{NR}_5\text{R}_6$ ,

wherein,

$R_5$  and  $R_6$  are independently hydrogen,  $C_1-C_6$  alkyl,  $C_2-C_6$  alkenyl, or  $C_4-C_{10}$  aryl, and

$n$  is an integer of 1 to 2.

22. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $CH_2CH_3$ , and  $R$  is  $(CH_2)_nCOR_7$ ,

wherein,

$R_7$  is hydroxy,  $C_1-C_6$  alkyl,  $C_2-C_6$  alkenyl, or  $C_4-C_{10}$  aryl, and

$n$  is an integer of 2 to 4.

23. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $C_1-C_{30}$  alkyl.

24. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $C_1-C_{20}$  alkyl.

25. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $C_2-C_{22}$  alkenyl.

26. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $C_2-C_6$  alkenyl.

27. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $C_4-C_{30}$  aryl.

28. The di-ester of claim 2, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $C_4-C_{20}$  aryl.

29. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $(CH_2)_nOR_5$ ;

wherein,

$R_5$  is  $C_1-C_6$  alkyl,  $C_1-C_6$  alkenyl, or  $C_4-C_{10}$  aryl, and

$n$  is an integer of 1 to 2.

30. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $(CH_2)_nSR_5$ ,

wherein,

$R_5$  is  $C_1-C_6$  alkyl,  $C_1-C_6$  alkenyl, or  $C_4-C_{10}$  aryl, and  
 $n$  is an integer of 1 to 2.

31. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $(CH_2)_nNR_5R_6$ ,

wherein,

$R_5$  and  $R_6$  are independently hydrogen,  $C_1-C_6$  alkyl,  $C_1-C_6$  alkenyl, or  $C_4-C_{10}$  aryl,  
and  
 $n$  is an integer of 1 to 2.

32. The di-ester of claim 1, wherein each of  $R_1$ ,  $R_2$  and  $R_3$  is H,  $R_4$  is  $Si(CH_3)_2C(CH_3)_3$ , and  $R$  is  $CH_2)_nCOR_7$ ,

wherein,

$R_7$  is hydroxy,  $C_1-C_6$  alkyl,  $C_2-C_6$  alkenyl, or  $C_4-C_{10}$  aryl, and  
 $n$  is an integer of 2 to 4.

33. The di-ester of claim 1, wherein  $R_1$  is  $CH_2N(CH_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and  $R$  is  $C_1-C_{30}$  alkyl.

34. The di-ester of claim 2, wherein  $R_1$  is  $CH_2N(CH_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and  $R$  is  $C_1-C_{20}$  alkyl.

35. The di-ester of claim 1, wherein  $R_1$  is  $CH_2N(CH_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and  $R$  is  $C_2-C_{22}$  alkenyl.

36. The di-ester of claim 2, wherein  $R_1$  is  $CH_2N(CH_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and  $R$  is  $C_2-C_6$  alkenyl.

37. The di-ester of claim 1, wherein  $R_1$  is  $CH_2N(CH_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and  $R$  is  $C_4-C_{30}$  aryl.

38. The di-ester of claim 2, wherein  $R_1$  is  $CH_2N(CH_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and  $R$  is  $C_4-C_{20}$  aryl.

39. The di-ester of claim 1, wherein  $R_1$  is  $\text{CH}_2\text{N}(\text{CH}_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(\text{CH}_2)_n\text{OR}_5$ ,

wherein,

$R_5$  is  $\text{C}_1\text{--C}_6$  alkyl,  $\text{C}_2\text{--C}_6$  alkenyl, or  $\text{C}_4\text{--C}_{10}$  aryl, and

n is an integer of 1 to 2.

40. The di-ester of claim 1, wherein  $R_1$  is  $\text{CH}_2\text{N}(\text{CH}_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(\text{CH}_2)_n\text{SR}_5$ ,

wherein,

$R_5$  is  $\text{C}_1\text{--C}_6$  alkyl,  $\text{C}_2\text{--C}_6$  alkenyl, or  $\text{C}_4\text{--C}_{10}$  aryl, and

n is an integer of 1 to 2.

41. The di-ester of claim 1, wherein  $R_1$  is  $\text{CH}_2\text{N}(\text{CH}_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(\text{CH}_2)_n\text{NR}_5\text{R}_6$ ,

wherein,

$R_5$  and  $R_6$  are independently hydrogen,  $\text{C}_1\text{--C}_6$  alkyl,  $\text{C}_1\text{--C}_6$  alkenyl, or  $\text{C}_4\text{--C}_{10}$  aryl, and

n is an integer of 1 to 2.

42. The di-ester of claim 1, wherein  $R_1$  is  $\text{CH}_2\text{N}(\text{CH}_3)_2$ , each of  $R_2$ ,  $R_3$  and  $R_4$  is H, and R is  $(\text{CH}_2)_n\text{COR}_7$ ,

wherein,

$R_7$  is hydroxy,  $\text{C}_1\text{--C}_6$  alkyl,  $\text{C}_2\text{--C}_6$  alkenyl, or  $\text{C}_4\text{--C}_{10}$  aryl, and

n is an integer of 2 to 4.

43. A method to inhibit the enzyme topoisomerase I comprising administering a composition comprising at least one di-ester of claim 1.

44. A method to inhibit the enzyme topoisomerase I comprising administering a composition comprising at least one di-ester of claim 2.

45. A method to treat cancer in a patient comprising administering a composition comprising at least one di-ester of claim 1 to said patient in an effective amount to treat said cancer.

46. A method to treat cancer in a patient comprising administering a composition comprising at least one di-ester of claim 2 to said patient in an effective amount to treat said cancer.

47. The method of claim 45, wherein said cancer is lung, breast, colon, prostate, melanoma, pancreas, stomach, liver, brain, kidney, uterus, cervix, ovaries, urinary tract, gastrointestinal, or leukemia.

48. The method of claim 46, wherein said cancer is lung, breast, colon, prostate, melanoma, pancreas, stomach, liver, brain, kidney, uterus, cervix, ovaries, urinary tract, gastrointestinal, or leukemia.

49. The method of claim 45, wherein said cancer is solid tumor or blood born tumor.

50. The method of claim 46, wherein said cancer is solid tumor or blood born tumor.

51. The method of claim 45, wherein said composition is administered orally, parenterally, intramuscularly, transdermally or by an airborne delivery system.

52. The method of claim 46, wherein said composition is administered orally, parenterally, intramuscularly, transdermally or by an airborne delivery system.

53. The method of claim 45, wherein said composition is a nanoparticle containing said at least one di-ester of camptothecin.

54. The method of claim 46, wherein said composition is a nanoparticle containing said at least one di-ester of camptothecin.